REMARKS/ARGUMENTS

The October 19, 2002 Office Action objected to claim 18, rejected claims 1, 3 - 11 and 13 - 18 under 35 U.S.C. § 112 and rejected claims 1, 4 - 6, 10 - 11, 13 - 16 and 18 under 35 U.S.C. § 102(e).

On February 27, 2003 Applicants' attorneys and Inventor Su-Chun Zhang interviewed Examiner Nguyen and Examiner David Guzo at their offices in Washington, D.C. Applicants thank the Examiners for the courtesy of their time and for their helpful suggestions. Applicants and their attorneys and the Examiners agreed that Applicants would amend the claims in response to the § 112 rejections proffered in the above-identified Office Action, file an RCE, and enclose a Declaration signed by Inventor Zhang in response to the § 102(e) rejection. Applicants have done so.

RCE Filing

Applicants note that they have submitted an RCE request herein. Applicants have also submitted a Petition and Fee for Two Months Extension of Time so the RCE will be filed in an appropriate time frame.

Claim Objections:

Claim 18 is objected to as being a substantial duplicate of claim 6. Applicants have cancelled claim 18.

§ 112 Rejections

Claims 1 and 14 are rejected under 35 U.S.C. § 112, second paragraph on the ground that it is unclear what is encompassed by the phrase "cells are characterized by rosette formations." As Applicants discussed with the Examiners in their Office interview, Applicants have amended the claims to specify that the precursor cells form rosette formations.

Claim 3 has been rejected as lacking antecedent basis. This has been corrected.

§ 102 Rejection

Claims 1, 4 - 6, 10 - 11, 13 - 16 and 18 are rejected under 35 U.S.C. § 102(e) as being anticipated by Carpenter (WO 01/88104).

As Applicants and their attorney pointed out to the Examiners in their February 27, 2003 interview, the Carpenter method and the method of the present invention have a different objective and result in cells with a different pattern of differentiation.

As a preliminary matter, Applicants indicate that they have enclosed a Declaration of Dr. Su-Chun Zhang with two attachments. Attachment A (Table 1) is a comparative table of the Carpenter versus the Zhang method. Attachment 2 is a copy of "Mammalian Neural Stem Cells", *Science* 287, 25 February 2000. Applicants point to Fig. 1, an illustration proposing the classes of mammalian stem cells that can give rise to neurons. It was this figure that Dr. Zhang used in his conversation with the Examiners during the office interview of February 27, 2003. The notes on the page are Professor Zhang's handwritten notes made during the interview.

The enclosed Declaration of Inventor Su-Chun Zhang indicates that the Carpenter, et al. disclosure relates to obtaining neural progenitor cells that are restricted in their differentiation to either neurons or glial cells while the method of the present invention is designed to obtain a synchronized population of neural precursor cells that can give rise to neurons, astrocytes and oligodendrocytes.

Dr. Zhang points out in paragraph 5 that in the Carpenter, et al. protocol, 10 μM of retinoic acid is added to the culture wherein in the Zhang, et al. protocol, there is no retinoic acid. Retinoic acid is a strong morphogen and strongly promotes differentiation. Dr. Zhang also points out

at paragraph 6 that the incubation cocktail is different in the sense that the Carpenter, et al. protocol uses multiple growth factors as opposed to a single factor. Hence, under the influence of these contradicting factors, the Carpenter, et al. culture results in a mixture of neural cells that ranges from progenitors to mature neurons.

In contrast, the method of the present invention induces a synchronized population of neural precursor cells without the presence of mature neurons. Thus, the method of the present invention leads to a synchronized population that organizes into neural tube-like rosette formation. As Dr. Zhang points out in paragraph 8, rosette formation is a characteristic feature of neural epithelial cells. Neural cells differentiated from Carpenter's protocol do not form rosette structures.

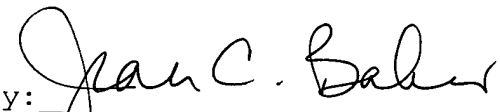
Applicants have enclosed a two month extension of time. If further fees are believed necessary, please charge Deposit Account 17-0055.

The Commissioner is authorized to charge any fees under 37 CFR § 1.17 that may be due on this application to Deposit Account 17-0055. The Commissioner is also authorized to treat this amendment and any future reply in this matter requiring a petition for an extension of time as incorporating a petition

for extension of time for the appropriate length of time as provided by 37 CFR § 136(a)(3).

Respectfully submitted,

Su-Chun Zhang, et al.

By: 

Jean C. Baker
Quarles & Brady LLP
Reg. No. 35,433
Attorney for Applicant
411 East Wisconsin Avenue
Milwaukee, WI 53202-4497
414/277-5709

5392723.1

Table 1

	Carpenter	**Zhang**
Initial cells	hES	hES
Objective	Neuronal or glial progenitors	Neural stem cells (can give rise to both neurons and glia)
Embryoid body	Retinoic acid treatment, 4 days	No retinoic acid treatment, 4 days
Differentiation medium	DMEM/F12, N2 FGF2 (bFGF, 10 ng/ml) EGF, PDGFaa, IGF-1, B27 (at least 2 growth factors) 3 days	DMEM/F12, N2 FGF2 (10-20 ng/ml) (A single factor is sufficient)
Neural cells morphology	Neuronal morphology (p388) No rosette formation	Neuroepithelial morphology rosette formation
Antigenic expression	A2B5, PSA-NCAM, b-tubulin, MAP-2 (p389)	Nestin, PSA-NCAM No b-tubulin, MAP-2
Separation	Magnetic separation	Enzymatic and Adhesion
Purity	A2B5: 48-93% PSA-NCAM: 25-72%	Nestin: >95%
Resulting differentiation outcome	PSA-NCAM cells: restricted to neuronal formation (p391) A2B5 cells: form neurons, fewer form GFAP+cells (p391)	Isolated nestin+cells generate neurons, astrocytes, and oligodendrocytes